REMARKS

Applicants respectfully thank Examiner Tran for the telephonic interview granted on October 2, 2003. The present claim amendments and arguments are further to our discussion. As agreed upon in the interview, the Applicants would welcome a telephone call from the Examiner to discuss any matter related to the invention or this Amendment and Response.

By this Amendment and Response, claims 1 and 21-38 have been amended and claims 1-15 and 21-38 are pending in the present application. As indicated in the following discussion, the support for the amendments can be found throughout the application as filed, for example at paragraphs 7, 10, and 29 of the application as filed.

To the extent not superceded by Amendments or Remarks made herein, Applicants incorporate by reference their Remarks made in the Amendment and Response filed February 27, 2003. Although Applicants believe the previously pending claims were patentable over the cited art of record for the reasons presented in the Amendment and Response filed February 27, 2003, the present claim amendments and the following remarks are presented to further the prosecution of this case and obtain a prompt allowance of the present claims. Accordingly, favorable reconsideration of the pending claims is respectfully requested.

1. Claim Amendments Unrelated to the Patentability of the Claims

Claims 21 and 33 have been amended and restructured for clarity to more clearly recite "A sustained release orally administered specimen" as opposed to "A sustained release composition for use as an excipient of an orally administered specimen." In addition, the recited cellulose and maltodextrin are now grouped collectively as "an excipient portion" such that the orally administered

specimen comprises an excipient portion (cellulose and maltodextrin) and a bioactive substance or glucosamine-based substance.

This amendment for clarity is in line with the well known definition of excipient. *See, The American Heritage® Dictionary of the English Language* (4th ed.. 2000) ("An inert substance used as a diluent or vehicle for a drug."); *Stedman's Online Medical Dictionary,* (27th ed.) ("A more or less inert substance added in a prescription as a diluent or vehicle or to give form or consistency when the remedy is given in pill form; e.g., simple syrup, vegetable gums, aromatic powder, honey, and various elixirs."). In the present invention, the cellulose and maltodextrin are an excipient in that they are each "[a]n inert substance used as a diluent or vehicle for a drug."

2. Rejections Under 35 U.S.C. §§ 102 & 103

a. General Comments

Before further addressing any specific claims or the outstanding rejections, Applicants believe it would be helpful at this provide some background information that illuminates, in part, the present invention. In that regard, Applicants direct the Examiner to paragraphs 7, 10, and 29 of the specification:

> **[07]** It is an object of the present invention to provide compositions for oral administration of substances including dietary supplements and medicines **such that the detrimental side effects of these substances are minimized or even eliminated**.
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> * * *
>
> **[010]** To achieve the foregoing objects, and in accordance with the invention as embodied and broadly described herein, compositions according to the present invention comprise combinations of maltodextrin and cellulose. **The cellulose is preferably used in the form of powdered cellulose, and its combination with maltodextrin provides gelling effects and it slows the disintegration of the tablet**,

> thus contributing to the sustained release of the medicine or supplement in the tablet. In addition, the gelling effects prevent the direct contact with the stomach wall of a substantial amount of the possibly irritant medicine or supplement.
>
> * * *
>
> **[029]** An embodiment of the sustained release composition according to the present invention was incorporated into a glucosamine/MSM tablet in the form of a preparation that was obtained by **mixing** about 40.0% **GLUCOSAMINE** SUL. 68/95% GRAN. KCL 30 MESH, about 26.6% METHYL SULFONYL METHANE (MSM), about 17.2% **MALTRIN** M510 (GPC), about 7.1% **CELLULOSE**, POWDERED EXP 9250 . . .

(emphasis added). From these passages it is evident that the inventive compositions are used to minimize the harmful side effects of dietary supplements and medicines. These inventive compositions include a mixture of cellulose and maltodextrin, the combination of which "provides gelling effects and [] slows the disintegration of the tablet." It is this slow disintegration of the tablet, or "sustained release," in combination with the gelling, that keeps the dietary supplement (e.g. glucosamine) or medicine from irritating the stomach wall.

Other examples of usage of the term "slow release" that illuminate its meaning include: "[t]he cellulose is preferably used in the form of powdered cellulose, and its combination with maltodextrin provides gelling effects and it **slows the disintegration of the tablet, thus contributing to the sustained release** of the medicine or supplement in the tablet (para. 10); and "[t]he present invention is directed to sustained release compositions that **slow the disintegration of the delivery specimen**" (para. 16) (emphasis added). *See also* para. 40, ("[T]he sustained release composition of the present invention effectively provides a release medium and release mechanism such that the active substance is gradually and continuously incorporated into the receiving environment.").

b. Claims 1 and 7-11

Claims 1 and 7-11 have been rejected under 35 U.S.C. §§ 102(b) and 103 as being unpatentable over United States Patent No. 5,470,581 issued to Grillo et al. ("*Grillo*") for the reasons set forth on pages 2-3 of the Office Action.

Present claim 1 recites, among other things, "A sustained release composition for use as an excipient of an orally administered specimen containing a bioactive substance. . . wherein, upon mixing with a bioactive substance in an orally administered substance, the cellulose and the maltodextrin slow the disintegration of the orally administered specimen to provide a sustained release of the bioactive substance."

One purpose and advantage of mixing the cellulose and the maltodextrin throughout the specimen, and not merely using them as a coating, is clearly stated in paragraph 10 of the application as filed:

> The cellulose [in] combination with maltodextrin provides gelling effects and . . . *slows the disintegration of the tablet*, thus contributing to the *sustained release of the medicine or supplement in the tablet*. In addition, the gelling effects prevent the direct contact with the stomach wall of a substantial amount of the possibly irritant medicine or supplement. (emphasis added)

Hence, by more definitively reciting "the cellulose and the maltodextrin slow the disintegration of the orally administered specimen to provide a sustained release of the bioactive substance," Applicants respectfully submit that the present claim 1 clearly is directed to mixtures and does not permit "the film forming around the dosage form," as characterized in the Office Action in rejecting claim 1 over *Grillo*. Office Action, p. 6.

In contrast, *Grillo* discloses a method of *coating* pharmaceutical tablets and the like. *See, e.g.*, Abstract of *Grillo* ("A method of coating substrates."); col. 1, ll. 10-12 ("This invention is in the

field of aqueous film coating . . . and is specifically concerned with providing coatings."); col. 3, l. 43 ("[A] number of HPMC coating films were made."). The advantages cited by Grillo include: "a stronger coating" and "excellent adhesive qualities, enhanced gloss characteristics and reduced incidence of cloudiness." Col. 5, ll. 10-14, and 36-38. These advantages are largely irrelevant to the present invention's sustained release tableting compositions. Further, *Grillo* requires the use of a plasticizer, such as polyethylene glycol (*see* col. 2, ll. 6-8), and water, components necessary to form a coating suspension but not required for use with sustained release tablets.

Additionally, despite *Grillo's* teaching of a coating that includes, among other things, maltodextrin and cellulose polymers, such compositions as taught by *Grillo* do not provide for sustained release and would not protect a stomach wall from direct contact with a medicine or supplement. Hence, *Grillo* is clearly directed to teaching a "coating" or "coating film" as opposed to a sustained release compound that is "distributed throughout the orally administered specimen" as recited in claim 1.

Accordingly, Applicants respectfully submit that claim 1 and any claim depending directly or indirectly therefrom, is neither disclosed nor anticipated by *Grillo*. Claims 7-11 depend from claim 1, and therefore, include the limitations therein. As a result, Applicants believe that claims 7-11 are patentable over *Grillo* for at least the reasons presented with respect to claim 1. It is respectfully submitted that the rejections of claims 1 and 7-11 based on U.S.C. □102 have been overcome and should now be withdrawn.

In the Office Action, claims 1 and 7-11 were also rejected under 35 U.S.C. § 103 as being unpatentable based on obviousness to one of ordinary skill in the art to modify *Grillo's* composition with expectation of at least similar result.

1. Obviousness Rejections in General

Applicants respectfully submit that a *prima facie* case of obviousness has not been established for the present claims 1 and 7-11. Under M.P.E.P. □2143, a *prima facie* case of obviousness requires establishing three (3) elements:

(1) some suggestion or motivation in the cited reference to modify the reference;

(2) a reasonable expectation of success; and

(3) an explicit teaching in the combination or at least a suggestion, of all the claim limitations at issue.

The fact that the reference can be modified is not sufficient to establish obviousness, unless the prior art in addition suggests the desirability of the modification. M.P.E.P. □2143.01. The teaching or suggestion to make the modification must be found in the prior art, and not based on applicants disclosure. M.P.E.P. □2143. According to M.P.E.P. □2142, it is impermissible to use hindsight to find the motivation to make the modification. Instead, the reference must "expressly or impliedly suggest the claimed invention." In other words, there must exist some teaching, suggestion or motivation to do so in, either the reference, or in knowledge generally available to one of ordinary skill in the art. M.P.E.P. □2143.01.

Grillo is entirely focused on coatings and their respective properties. There is no suggestion or motivation anywhere in *Grillo* to move from making "coatings" and optimizing the properties of the "coating films" to making "[a] sustained release composition for use as an excipient of an orally administered specimen containing a bioactive substance." Cl. 1. Further, the proposed modification would make *Grillo* unsatisfactory for its intended purpose of applying "coatings." As a result, there would be no reasonable expectation of success in making the change. Applicants therefore

respectfully submit that hindsight is impermissibly being used in making the obviousness rejection of claims 1 and 7-11 based on *Grillo*.

Accordingly, Applicant respectfully submits that independent claim 1, as amended and presented herein, and any claims depending directly or indirectly therefrom, is neither disclosed nor obvious variations of the structure in *Grillo*. Because claims 7-11 depend, directly or indirectly, from claim 1, as amended and presented herein, for the reasons stated above relative to claim 1, it is respectfully submitted that claims 7-11 are neither disclosed nor obvious variations of the structures disclosed or suggested in *Grillo*. Applicants, therefore, respectfully request that the rejections of claims 1 and 7-11 under 35 U.S.C. §§ 102 and 103 be withdrawn.

c. Claims 21-23 and 29-32

Claims 21-23 and 29-32 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Grillo* and United States Patent No. 5,128,143 issued to Baichwal et al. ("*Baichwal*") for the reasons set forth on pages 3-4 of the Office Action. The Office Action notes that "Grillo does not teach the sustained release time period," and then goes on to explain how *Baichwal* overcomes this deficit. See Office Action, pp. 2-3.

Present claim 21 recites, among other things, "the maltodextrin and the cellulose provide in an aqueous medium the sustained release of the bioactive substance for a time period" and "wherein the cellulose and the maltodextrin are mixed with the bioactive substance throughout the orally administered specimen such that, upon ingestion, the orally administered specimen gels to prevent direct contact between a substantial amount of the bioactive substance and a stomach wall." As previously discussed, *Grillo* is entirely focused on coatings and optimizing the properties of the

"coating film," including tensile strength, modulus of elasticity, clarity, and tensile strength. *Grillo*, col. 5, ll. 15-28. To that end, *Grillo* requires the use of both a plasticizer and water, components unnecessary and incompatible for use in a powdered tablet. In addition, *Grillo* in no way teaches or suggests the use of cellulose and maltodextrin to obtain sustained release or gelling features. Accordingly, Applicants respectfully submit that claim 21 is also neither anticipated nor obvious over *Grillo* for the reasons presented above with respect to claim 1.

Baichwal cannot cure the deficiencies of *Grillo*. *Baichwal* teaches "a slow release pharmaceutical excipient comprising from about 20 to about 70 percent or more by weight of a hydrophilic material comprising a heteropolysaccharides (*e.g.* xanthan gum) and a polysaccharide material capable of cross-linking the heteropolysaccharides (*e.g.* a galactomannan) in the presence of aqueous solutions, and from about 30 to about 80 percent by weight of an inert pharmaceutical filler (*e.g.* the monosaccharide dextrose)." *Baichwal*, col. 4, ll. 15-23 (parentheticals added). *Baichwal* also teaches a slow release pharmaceutical excipient comprising "(I) a hydrophillic material comprising (a) a heteropolysaccharide; or (b) a heteropolysaccharide and a cross-linking agent capable of cross-liking said heteropolysaccharide; or (c) a mixture of (a), (b) and a polyscaccharide gum; and (II) an inert pharmaceutical filler comprising up to about 80 percent by weight of the tablet; and (III) an effective amount of therapeutically active ingredient." *Baichwal*, col. 4, ll. 52-60.

A *prima facie* case of obviousness of present claim 21 based on the combination of *Grillo* and *Baichwal* has not been established. As previously noted, under M.P.E.P. □2143, a *prima facie* case of obviousness requires establishing that there be some suggestion or motivation in the cited references to combine the reference teachings, that there be a reasonable expectation of success, and

that the combined references teach or suggest all the claim limitations. For the following reasons, Applicants respectfully submit that none of these criteria are met by the cited references.

Regarding the first two elements to establish a *prima facie* case of obviousness, Applicants hereby incorporate by reference their Remarks filed in the previous Amendment and Response dated February 27, 2003.

In addition, even if *Grillo* and *Baichwal* are combined, to which Applicants object, Applicants respectfully submit that the proposed combination does not teach all the recited limitations in present claim 21. More specifically, the cited references do not teach or suggest a sustained release orally administered composition comprising an excipient portion (cellulose, maltodextrin) and a bioactive substance "such that the maltodextrin and the cellulose provide in an aqueous medium the sustained release of the bioactive substance for a time period" and "wherein the cellulose and the maltodextrin are mixed with the bioactive substance throughout the orally administered specimen such that, upon ingestion, the orally administered specimen gels to prevent direct contact between a substantial amount of the bioactive substance and a stomach wall," as recited in claim 21.

In the present application, Applicants are not merely claiming the use of cellulose and maltodextrin in any form in orally administered compositions. Rather, it is by mixing cellulose and maltodextrin throughout orally administered specimens that the hereinabove noted advantages of sustained release compositions that gel upon ingestion and thereby prevent direct contact between a substantial amount of the administered medicament are obtained.

As previously noted, *Grillo* requires the use of a plasticizer and water to create a coating suspension and nowhere teaches any methods or compositions that would enable cellulose and

maltodextrin to function as a sustained release excipient. *Baichwal* is similarly deficient in that it teaches only the use of a heteropolysaccharide (xanthan gum), a polysaccharide capable of cross-linking the heteropolysaccharides (galactomannan) and optional inert filler (a monosaccharide such as dextrose). Hence, neither reference teaches or suggests that the combination of cellulose and maltodextrin would function as a sustained release excipient.

Accordingly, Applicants respectfully submit that independent claim 21, as amended and presented herein, and any claims depending directly or indirectly therefrom, is neither disclosed nor obvious variations of the structure in *Grillo* and *Baichwal* alone or in combination. Because claims 22-23 and 29-32 depend, directly or indirectly, from claim 21, as amended and presented herein, for the reasons stated above relative to claim 21, it is respectfully submitted that claims 22-23 and 29-32 are neither disclosed nor obvious variations of the structures disclosed or suggested in *Grillo* and *Baichwal*, alone or in combination. It is respectfully submitted that the rejection of claims 21-23 and 29-32 based on 35 U.S.C. □103 has been overcome and should be reconsidered and withdrawn.

d. Claims 2-6, 33, and 35-38

Claims 2-6, 33, and 35-38 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Grillo* and United States Patent No. 6,417,227 issued to Lord et al. ("*Lord*") for the reasons set forth on page 4 of the Office Action.

Present claim 33 recites, among other things, "the maltodextrin and the cellulose slow the disintegration of the orally administered specimen and thereby provide in an aqueous medium the sustained release of the glucosamine-based substance for a time interval such that the released glucosamine-based substance does not significantly irritate the recipient's stomach lining" and

"wherein the cellulose and the maltodextrin are mixed with the glucosamine-based substance throughout the orally administered specimen such that, upon ingestion, the orally administered specimen gels to prevent direct contact between a substantial amount of the glucosamine-based substance and a stomach wall and thereby acts as a stomach guard with respect to the glucosamine-based substance."

As previously discussed, *Grillo* is entirely focused on coatings and optimizing the properties of the "coating film," including tensile strength, modulus of elasticity, clarity, and tensile strength. *Grillo*, col. 5, ll. 15-28. To that end, *Grillo* requires the use of both a plasticizer and water, components unnecessary and incompatible for use in a powdered tablet. Accordingly, Applicants respectfully submit that claim 33 is also neither anticipated nor obvious over *Grillo* for the reasons presented above with respect to claim 1.

Lord cannot cure the deficiencies of *Grillo*. *Lord* discloses a method of delivery of cetyl myristoleate. More specifically, *Lord* teaches an "oral medicament comprising cetyl myristoleate and an enteric coating. The enteric coating is resistant to dissolution in the stomach but predisposed to dissolution in the intestine so as to prevent release of the cetyl myristoleate until the medicament is in the intestine." *Lord*, col. 2, ll. 44-48. *Lord* identifies a number of materials which can be used to form the enteric coating, but also states that "[t]he choice of enteric-coating materials is not of significance as long as release is delayed until the formulation reaches the small intestine." *Lord*, col. 8, ll. 8-19.

Hence, *Lord* does not teach or suggest a sustained release composition "wherein the cellulose and the maltodextrin are mixed with the glucosamine-based substance throughout the orally administered specimen" as recited in claim 33 or "wherein the cellulose and the maltodextrin are

mixed with the bioactive substance throughout the orally administered specimen," as recited in claim 1. As previously stated, one purpose and advantage of distributing the cellulose and the maltodextrin *throughout* the specimen, and not merely as a coating, is clearly stated in paragraph 10 of the application as:

> The cellulose [in] combination with maltodextrin provides gelling effects and . . . *slows the disintegration of the tablet*, thus contributing to the *sustained release of the medicine or supplement in the tablet*. In addition, the gelling effects prevent the direct contact with the stomach wall of a substantial amount of the possibly irritant medicine or supplement. (emphasis added).

In fact, the oral administration method identified in *Lord* is specifically utilizes a particular coating to prevent and delay *any* release until the dosage reaches the small intestine.

Accordingly, Applicants respectfully submit that independent claims 1 and 33, as amended and presented herein, and any claims depending directly or indirectly therefrom, are neither disclosed nor obvious variations of the structure in *Grillo* and *Lord* alone or in combination. Because claims 2-6, and 35-38, depend, directly or indirectly, from claims 1 and 33, as amended and presented herein, for the reasons stated above relative to claims 1 and 33, it is respectfully submitted that claims 2-6, and 35-38 are neither disclosed nor obvious variations of the structures disclosed or suggested in *Grillo* and *Lord*, alone or in combination. It is respectfully submitted that the rejection of claims 2-6, 33 and 35-38 based on 35 U.S.C. § 103 has been overcome and should be reconsidered and withdrawn.

e. Claims 12-15, 24-28 and 34

Claims 14, 15, and 34 have been rejected under 35 U.S.C. § 103(a) as being unpatentable

over Grillo in view of Lord and the Web page www.grainprocessing.com/food/malinfo.html ("*Grain Processing*") for the reasons set forth on pages 4-5 of the Office Action. The Office Action notes that Grillo and Lord are silent as to the teaching of the claimed maltodextrin, and then goes on to explain how *Grain Processing* overcomes this deficit. See Office Action, pp. 4-5.

Claims 24-28 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Grillo Baichwal* and *Lord* for the reasons set forth on page 5 of the Office Action. The Office Action notes that *Grillo* and *Baichwal* are silent as to the teaching of the claimed specific agent, and then goes on to explain how *Lord* overcomes this deficit. See Office Action, p. 5.

Claims 12 and 13 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Grillo* and U.S. Patent No. 6,069,172 to Bertini et al. ("*Bertini*") for the reasons set forth on pages 5-6 of the Office Action. The Office Action notes that *Grillo* does not teach the claimed cellulose polymer, and then goes on to explain how *Bertini* overcomes this deficit. See Office Action, pp. 5-6.

For the reasons presented hereinabove with respect to the independent claims 1, 21, and 33, none of *Grillo*, *Lord*, and *Baichwal* teach or suggest the foregoing discussed limitations of claims 1, 21, and 33. In addition, *Grain Processing* and *Bertini* cannot overcome these deficiencies.. *Grain Processing* merely discloses the characteristics of various edible maltodextrin compositions and *Bertini* is cited for disclosing the polymerization of cellulose.

Accordingly, Applicants respectfully submit that independent claims 1, 21, and 33, as amended and presented herein, and any claims depending directly or indirectly therefrom, are neither disclosed nor obvious variations of the structure in *Grillo*, *Lord*, and *Baichwal*, *Grain Processing* or *Bertini* alone or in combination. Because claims 14, 15, and 34; 24-28; and 12 and 13, depend, directly or indirectly, from claims 1, 21 and 33, as amended and presented herein, for the reasons

stated above relative to claims 1, 21, and 33, it is respectfully submitted that claims 14, 15, and 34; 24-28; and 12 and 13are neither disclosed nor obvious variations of the structures disclosed or suggested in *Grillo*, *Lord*, and *Baichwal*, *Grain Processing* or *Bertini* alone or in combination. It is respectfully submitted that the rejection of claims 14, 15, and 34; 24-28; and 12 and 13 based on 35 U.S.C. □103 has been overcome and should be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing, Applicants respectfully request favorable reconsideration and allowance of the present claims. In the event the Examiner finds any remaining impediment to the prompt allowance of this application that could be clarified by a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney.

Dated this 6th day of October, 2003.

Respectfully submitted,

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